

HOW CLOSE IS fMRI TO PROVIDING THE MEMORY COMPONENT OF THE WADA TEST?

Functional MRI Predicts Postsurgical Memory following Temporal Lobectomy

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Temporal lobectomy is an effective therapy for medically refractory temporal lobe epilepsy (TLE), but may be complicated by amnesic syndromes. Therefore, presurgical evaluation to assess the risk/benefit ratio for surgery is required. Intracarotid amobarbital testing (IAT) is currently the most widely used method for assessing presurgical memory lateralization but is relatively invasive. Over the past decade, functional MRI (fMRI) has been shown to correlate with IAT for language lateralization and for memory lateralization in a small number of patients. This study was carried out to compare fMRI during memory encoding with IAT testing for memory lateralization and to assess the predictive value of fMRI during memory encoding for postsurgical memory outcome. Thirty-five patients with refractory TLE undergoing presurgical evaluation for temporal lobectomy and 30 normal subjects performed a complex visual scene-encoding task during fMRI scanning at 1.5 T by using a 10-min protocol. Encoding performance was evaluated with subsequent recognition testing. Twenty-three patients also completed the same task again outside the scanner, an average of 6.9 months after surgery. A region of interest

(ROI) analysis was used to quantify activation within hippocampal and a larger mesial temporal lobe ROI consisting of hippocampus, parahippocampus, and fusiform gyrus (HPF), as defined by a published template. Normal subjects showed almost symmetrical activation within these ROIs. TLE patients showed greater asymmetry. Asymmetry ratios (ARs) from the HPF ROI correlated significantly with memory lateralization by IAT. HPF ARs also correlated significantly with memory outcome, as determined by a change in scene recognition between presurgical and postsurgical trials. When absolute activation within the HPF ROI was considered, a significant inverse correlation between activation ipsilateral to temporal lobectomy and memory outcome was observed, with no significant correlation in the contralateral HPF ROI. Although further technical improvements and prospective clinical validation are required, these results suggest that mesial temporal memory activation detected by fMRI during complex visual scene encoding correlates with postsurgical memory outcome and supports the notion that this approach will ultimately contribute to patient management.

Pre-operative Verbal Memory fMRI Predicts Post-operative Memory Decline after Left Temporal Lobe Resection

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Functional MRI (fMRI) of cognitive tasks depends on technology widely available in the clinical sphere but has yet to show a role in the investigation of patients. We report here the first demonstration of a clinically valuable role for cognitive fMRI. Temporal lobe epilepsy (TLE) is commonly caused by hippocampal sclerosis and is frequently resistant to drug treatment. Surgical resection of the left hippocampus in this setting can cure seizures but may produce significant verbal memory decline, which is hard to predict. We report 10 right-handed TLE patients with left

hippocampal sclerosis who underwent left hippocampal resection. We compared currently used data for the prediction of postoperative verbal memory decline in such patients with a novel fMRI assessment of verbal memory encoding. Multiple regression analyses showed that fMRI provided the strongest independent predictor of memory outcome after surgery. At the individual subject level, the fMRI data had high positive predictive value for memory decline.

COMMENTARY

Evaluating the risk of memory loss is a key function of the Wada test, along with lateralization of language dominance. Because the Wada test is invasive, there has long been an interest in replacing it as a routine presurgical test with a less-invasive technique. Functional MRI (*fMRI*) and magnetoencephalography have been the key candidates in the exploration of an alternate diagnostic tool. Because *fMRI* is more widely available, it may be the most likely replacement. Accumulating evidence shows that *fMRI* is quite reliable in identifying language dominance. It agrees with the Wada test on side of language dominance, and the only discrepancies occur when one test suggests bilateral language representation and the other unilateral dominance (1–3). However, the evaluation of memory by *fMRI* has lagged behind its use in the evaluation of language dominance. Three recent articles, including those by Rabin and colleagues as well as by Richardson and colleagues, offer promise that *fMRI* could eventually serve the memory function of the Wada test (4).

The memory test that Rabin and colleagues used was the encoding of a complex visual scene, which patients were asked to memorize. It was surprising that this task activated mesial temporal structures almost symmetrically; the authors speculated that both verbal and nonverbal strategies are used for encoding. When examining absolute activation, only ipsilateral activation in an expanded mesial temporal region of interest significantly correlated with postoperative memory loss, whereas contralateral mesial temporal activation had no predictive value. This study, therefore, supports the functional adequacy model (which proposes that postoperative memory decline depends on how much memory function the ipsilateral hippocampus supports) but not the functional reserve model (which proposes that contralateral memory function predicts postoperative memory outcome).

Even though a correlation was found between expanded mesial temporal asymmetry ratios and Wada memory lateralization, it was not possible to make reliable, individual predictions of Wada memory lateralization from *fMRI* asymmetry ratios. In predicting postoperative memory decline, the study primarily used scores on the complex visual scene–encoding task, the same test used for the *fMRI* task. This procedure undoubtedly helped strengthen the correlation between *fMRI* activation and memory change. However, when standard memory tests were examined, *fMRI* asymmetry ratios correlated with change in memory scores only for patients with right temporal lobe epilepsy (TLE). Verbal memory is considered to be most at risk with temporal lobectomy, specifically after dominant resection. Therefore, learning to predict postoperative verbal memory decline for patients with left TLE is crucial.

It is possible that the *fMRI* method of Rabin and colleagues can be fine-tuned to provide a more powerful predictive value. The authors discuss at length the potential for technical advances in activation of the mesial temporal region, a region with physical characteristics that result in decreased blood oxygen level–dependent sensitivity. In addition, some evidence suggests that successful encoding is associated with greater *fMRI* activation (5); therefore, a study designed to image selectively just these successful encodings may strengthen the findings.

Richardson and colleagues studied a selected group of 10 patients with left TLE and left hippocampal sclerosis, who later underwent left hippocampal resection. The investigators used a verbal memory task in which patients were given a list of words that they were asked to classify as living or nonliving objects. Patients were not asked to remember the words but were later tested on their recollection of these words. The *fMRI* imaging data analysis used an event-related design, contrasting the encoding of clearly remembered words versus words that seemed only somewhat familiar. Verbal memory was measured preoperatively and 3 months postoperatively, by using a memory task different from that used for the *fMRI*. The left–right difference in hippocampal encoding activity correlated strongly with postoperative verbal memory change. The investigators found that *fMRI* was not only highly predictive of postoperative verbal memory change in patients with left TLE but also was a stronger independent predictor of memory outcome than two other confirmed predictive measures, preoperative verbal memory and left hippocampal volume. However, the study did not compare the *fMRI* task with the Wada test.

The Richardson et al. study demonstrated that with sophisticated analysis, memory *fMRI* has a tremendous predictive potential. The method should now be validated in a larger number of patients with more variable pathology and should be compared with the Wada test. The best prediction of memory outcome may require different tasks or batteries of tasks during *fMRI* with dominant and nondominant TLE patients, even though the technique used by Rabin and colleagues is attractive as a single task that can activate both mesial temporal regions.

Good reason exists to believe that the use of *fMRI* to predict postoperative memory outcome will one day be a satisfactory alternative to the Wada test as part of the routine presurgical evaluation. In the process of developing *fMRI* as a viable diagnostic tool for predicting postsurgical memory and language outcomes, there is an opportunity to reach a consensus on a universal testing technique and battery of tests and, thus, to avoid the problem of lack of standardization that has long plagued the Wada test.

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